Remarks

Claims 1-67 are pending in this application, however, claims 7, 10, 12, 16-20, 24-62, 64, 66 and 67 have been withdrawn from consideration as non-elected and are canceled herein. The Office has examined claim 65 rather than claim 64 with Group I and has included claim 11 in Group I. Applicants reserve the right to prosecute the subject matter of the canceled claims in a divisional application.

Claims 1-6, 8, 9, 11, 13-15, 21-23, 63 and 65, directed to methods involving SXR antagonists, have been considered by the Office. These claims are canceled and replaced with new claims 68-78 in this amendment. Applicants have canceled the pending claims and present new claims which recite a method comprising administering Ecteinascidin-743. Applicants reserve the right to prosecute the canceled subject matter in a continuation application.

Applicants note with appreciation the Office's acknowledgment of Applicants' claim for domestic priority.

The Office requests submission of new corrected drawings in view of the draftsperson's comments stated on form PTO-948 attached to the Office Action. Applicants submit formal drawings herewith.

The Office has rejected claims 1-6, 8, 9, 11, 13-15, 21-23, 63 and 65 under 35 U.S.C. §112, first paragraph, as containing subject matter not described in the specification so as to convey to the skilled person that applicants had possession of the claimed invention. The basis for the rejection is an allegation that the disclosure does not support the broad genus of methods of altering SXR activity or the broad number of compounds that agonize SXR.

The Office has conceded at page 5 of the Office Action that the specification describes Ecteinascidin-743 as an antagonist for SXR.

The current claims are fully supported by the specification, for example in Example 8, which demonstrates that ET-743 antagonizes SXR action in CV-1 cells and represses MDR1 transcription, and in paragraphs 14 and 19, which refer to minimal cytotoxicity. The sub-cytotoxic amounts applicants claim are below the dose an oncologist would use when treating cancer. ET-743 has been used in humans, and the specification provides examples using models well known in the art.

Applicants respectfully submit that the specification fully describes the methods claimed in the amended claims and therefore request that the rejection on grounds of inadequate written description be withdrawn.

The Office has rejected claims 1-6, 8, 9, 11, 13-15, 21-23, 63 and 65 under 35 U.S.C. §112, first paragraph as containing subject matter not enabled by the specification. As discussed above, Applicants have amended the claims, which now recite a method comprising administering Ecteinascidin-743. Enabling support for the claims can be found throughout the specification and particularly in Example 8 and in paragraphs 74 and 79.

In the rejection, the Office has focused on the perceived extreme breadth of the claims As discussed above, the claims have been amended. In addition, the Office remarks that cell cultures are not predictive because, "cell culture provides no information about whether a drug will make it to tumor sites." Applicants respectfully submit that this concern does not apply in the present invention. ET-743 is being used in amounts with minimal cytotoxic effects and therefore is not affecting tumors. Second, the method of this invention is not an anti-cancer therapy, so the ability of the agent to reach tumors is of no importance.

ET-743 has been discovered to modify SXR and to thereby affect drug metabolism. This is a general metabolic effect that affects other drugs' metabolism, not a tumor-specific one. It does not depend on cytotoxicity in tumors or in other cells. Applicants submit that the model systems used in the specification, coupled with what is known in the art concerning the effectiveness of ET-743 as it has been used in the past, would be recognized as predictive by skilled persons concerning the results which have been shown, i.e., altering pharmacokinetics and drug metabolism.

Applicants further submit that, given the guidance in the specification, the skilled person would not doubt that the results are achievable and can be accomplished without undue experimentation. SXR was shown to affect MDR1 transcription, which is well known to mediate drug resistance. These effects are shown to translate to the intact organism by drugs such as paclitaxel and many others that cause drug resistance. Specific ET-743 concentrations are provided in the specification, and these concentrations do not have to occur inside tumors for the method to work. Applicants submit that the methods claimed are fully enabled, and therefore request that this rejection be withdrawn.

The Office has rejected (provisionally) claims 1-5, 8, 11, 14 and 21 under the judicially created doctrine of double patenting as being unpatentable over claims 1-5, 8, 11, 14 and 21 of co-pending Application number 09/905,989.

The Office bases this rejection on the perceived overbreadth of the claims. Applicants believe that the amendments submitted herewith obviate this rejection, and therefore request its withdrawal.

For the reasons discussed above, Applicants request favorable consideration and allowance of the application at this time.

RESPECTFULLY SUBMITTED,			
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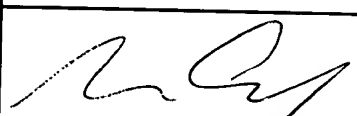
SIGNATURE		DATE	October 9,2003
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